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**The Role of Plant Agricultural Practices on Development of Antimicrobial Resistant Fungi  
Affecting Human Health: A Workshop**

**Statement of Task**

A planning committee of the National Academies of Sciences, Engineering, and Medicine will organize and conduct a public workshop series to shed light on: 1) the magnitude of environmentally induced/selected antimicrobial resistance (AMR) in agricultural practices worldwide, with a focus on plant crop production; 2) the practices that contribute to AMR in human pathogens, 3) surveillance strategies, and 4) mitigation strategies.

The public workshop series will feature invited presentations and discussions to explore the following questions:

- What is the magnitude of antifungal use in crop production in high-, middle- and low-income countries? How are such uses regulated?
- What are the mechanisms of AMR in plant pathogens and non-target environmental microbiota? How might this influence AMR in human pathogens?
- Which practices promote, prevent, or reduce the development of AMR in plant production environments, specifically in fungal pathogens? How does this affect risk of produce contamination with AMR pathogens?
- Are sampling and testing technologies for AMR surveillance in plant production systems adequate? What further evidence is needed to inform the use of antimicrobials worldwide? What further evidence is needed to understand the presence and effects of environmental AMR on human health?

The planning committee will organize the workshop, develop the agenda, select and invite speakers and discussants, and moderate or identify moderators for the discussions. One proceedings publication that reports on the presentations and discussions held during this workshop will be prepared by a designated rapporteur in accordance with institutional guidelines.

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**Project Context and Issues**

As the use of antimicrobials in agriculture has become a globally widespread and standard practice, the impacts on human, animal, and ecosystem health have become more pronounced. Antimicrobial resistance (AMR) is now one of the most pressing global health threats as microbes affecting humans, animals, and plants become less responsive to standard treatments (WHO, 2021). The use of antifungals in crop production is an area of great concern that has garnered the attention of global health entities such as the WHO and US HHS (WHO, 2021; HHS, 2021). Antifungal use in agriculture may promote the development of resistant fungi in the environment, with implications for human health. However, several questions remain as to the mechanisms that promote resistance, the effects of resistant fungi in the environment, and how this phenomenon might impact human health.

For decades, antimicrobials have been the cornerstone of control and treatment of many diseases in humans, animals, and plants alike. Fungal plant pathogens rarely infect animals and humans, although a few may cause disease in immune-compromised people or animals and several plant pathogenic fungi produce toxins that are harmful to humans and animals (van Overbeek, 2014; WHO, 2018). Antimicrobials are widely used in crop agriculture to protect plants from yield- or quality-limiting diseases. Recent estimates indicate that 20-40% of global crop production is lost to pre- and post-harvest diseases and pests, with climate change predicted to worsen this destruction (Savary, 2019; FAO, 2021). Fungi and oomycetes cause the majority of plant diseases and antifungal (fungicide) use is common in commercial crop production, landscapes, and home gardens. Limiting use of antimicrobials is key to mitigating AMR. However, steps to address this issue must be balanced with the need to address diseases and infections that threaten agricultural production. Food production, human health, and environmental stability depend on sustainable solutions for mitigating diseases that affect crops while reducing risk of AMR (FAO, 2016).

Although fungi can cause a spectrum of infections in humans, fungicides available for use systemically in human and veterinary medicine are limited. Of these, azoles are among the most common. Several different azole compounds and formulations are also used to control fungal diseases in plants. Widespread and long-term use of azoles on crops has resulted in selection of fungal phytopathogens (environmental isolates) that are resistant to them. Although the same agents are not employed for medical purposes, there is concern that the structural similarities between many of these compounds could result in cross-resistance with azoles reserved for use in human medicine. *Aspergillus fumigatus*, a fungus that is primarily treated by azoles, can cause aspergillosis (a lung infection) in humans. Azole-resistant *A. fumigatus* cases are much more difficult to treat and result in higher chances of patient death (CDC, 2021). This example, though more research is required, demonstrates how human health can be affected by AMR that may have arisen through agricultural practices.

In the U.S. and other high-income countries, approval for sale and use of pesticides including fungicides regulated based on efficacy evaluation and risk assessments for human health and the environment. In the U.S., statistics on pesticide use are generated from self-reporting by farmers responding to surveys or specific census requests ([www.nass.usda.gov](http://www.nass.usda.gov)). In contrast, regulations for pesticide use in low- and middle-income countries (LMICs) may be less stringent or not fully enforced due to lack of capacity. There is also little to no data published on the use of antibiotics and fungicides in LMICs. Additional surveillance is required to gain a better understanding of how pesticides are used globally, how their use influences AMR, and how

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human and plant pathogens interact to affect various aspects of health.

Antimicrobial resistance is problematic in crop production and various strategies have been developed to prevent or mitigate AMR development. A promising approach to limit the use of antimicrobials in conventional plant production systems and maintain their effectiveness is through the adoption of “Integrated Pest Management” (IPM), a systems approach designed to minimize economic losses to crops, as well as risks to people, animals, and the environment. The main components of IPM for plant diseases are 1) accurate diagnosis and monitoring, which can also include disease modeling and predictive systems to guide the timing of pesticide applications; 2) use of disease resistant crop varieties; 3) exclusionary practices that prevent the introduction of pathogens into a crop; 4) site selection and soil improvement to maximize plant health and minimize environmental factors that favor pathogens; 5) crop rotation and other cultural practices to prevent pathogen buildup; 6) use of biological and biorational products; and 7) judicious use of pesticides, including both antibiotics and fungicides.

While promising, the successful implementation of IPM and other approaches to counter the spread of AMR from agricultural practices hinge on several critical knowledge gaps. This includes accurate measurements of antimicrobial use and their regulatory guidance in different contexts (e.g., high-income countries vs LMIC), understanding of AMR mechanisms in the environmental microbiota that may be consequential for human health, and data on the effectiveness of current surveillance tools and systems. This public workshop series will provide an opportunity for researchers and policymakers working at the intersection of plant, animal, and human health to share the latest knowledge, advance the ongoing discussions, and develop ideas that can improve the mitigation strategies to contain the spread of AMR.

## References

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